We claim:

1. A composition comprising a DNA repair modulator that specifically binds to the sequence KKYIEIRKEAREAANGDSDGPSYM (SEQ. ID NO.:16) and inhibits non-homologous end joining.

2. The composition of claim 1, wherein the DNA repair modulator comprises a polypeptide.

3. The composition of claim 2, wherein the polypeptide comprises the sequence QVKLQESGAELVKPGASVKLSCKAFDYTFTTYDINWIKQRPGQGLWIGWIYPGS GNNKYNEKFKGKATLTADKSSRAAYMHLSSLTSEDSAVYFCAGGPLNMTGFDY WGQGTTVTVSSDIELTQSPSSMYASLGERVTITCKASQDINSYLSWFQQKPGKSP KTLIYRANRLVDGVPSRFSGSGSGQDYSLTISSLEYEDMGIYYCLQYDELPLTFGA GTKLEIKR (SEQ. ID NO.:17).

4. The composition of claim 1,wherein less than about 50% of DNA-PKcs enzymatic activity is inhibit by the DNA repair modulator.

5. A single chain antibody that specifically binds to DNA-PKcs in a region outside of the catalytic domain, wherein the single chain antibody includes complementarity determining regions FTTYDIN (SEQ. ID NO.:18), WIYPGSGNNKYNEKFKG (SEQ. ID NO.:19), GPLNMTGFDY (SEQ. ID NO.:20), KASQDINSYLS (SEQ. ID NO.:21), RANRLVD (SEQ. ID NO.:22), and LQYDELPLT (SEQ. ID NO.:23), in an immunoglobin framework.

6. A pharmaceutical composition comprising an DNA repair modulator, a prodrug thereof, or combination thereof, wherein the modulator inhibits DNA repair by specifically interacting with DNA-PKcs outside of the DNA-PKcs catalytic domain.

7. The pharmaceutical composition of claim 6, wherein the DNA repair modulator comprises a single chain antibody.

8. The pharmaceutical composition of claim 6, wherein the DNA repair modulator interacts with a region of DNA-PKcs having the sequence KKKYIEIRKEAREAANGDSDGPSYM (SEQ. ID NO.:16).

9. The pharmaceutical composition of claim 6, wherein the DNA repair modulator inhibits DNA end joining.

10. The pharmaceutical composition of claim 8, wherein the DNA repair modulator comprises a single chain antibody.

11. The pharmaceutical composition of claim 6, wherein the DNA repair comprises a repair of a double-strand break.

12. The pharmaceutical composition of claim 6, further comprising a pharmaceutically acceptable carrier, excipient, or diluent.

13. A pharmaceutical composition comprising a DNA repair modulator, a prodrug thereof, or a combination thereof, wherein the modulator interacts with a DNA repair polypeptide and sterically inhibits the DNA repair polypeptide.

14. The pharmaceutical composition of claim 13, wherein the DNA repair modulator comprises a single chain antibody.

15. The pharmaceutical composition of claim 13, wherein the DNA repair modulator interacts with a region of DNA-PKcs.

16. The pharmaceutical composition of claim 15, wherein the region of DNA-PKcs include the sequence KKKYIEIRKEAREAANGDSDGPSYM (SEQ. ID. NO. 16) or a portion thereof.

17. The pharmaceutical composition of claim 13,wherein the DNA repair modulator inhibits DNA end joining.

18. The pharmaceutical composition of claim 15, wherein the DNA repair modulator comprises a single chain antibody.

19. The pharmaceutical composition of claim 13, further comprising a pharmaceutically acceptable carrier, excipient, or diluent.

20. A method of screening for DNA repair modulators comprising:

(a) introducing a test compound into a plurality of cells;

(b) inducing breaks in genetic material of the plurality of cells; and

(c) selecting the test compound that modulates the ability to repair breaks in the genetic material compared to the ability or repair breaks in genetic material of control cells and binds to DNA-PKcs in a region outside of DNA-PKcs's catalytic domain.

21. The method of claim 20, wherein the test compound that inhibits the ability to repair breaks in the genetic material is selected.

22. The method of claim 20, wherein the test compound that promotes the ability to repair breaks in the genetic material is selected.

23. The method of claim 20, wherein the test compound is introduced into the plurality of cells in vivo or in vitro.

24. A cell-free assay for identifying DNA repair modulators comprising the steps of:

(a) combining a test compound with a reaction mixture, wherein the reaction mixture comprises a DNA ligase IV/XRCC4 complex, optionally other DNA DSB repair proteins, introduced in purified form or as a mixture in a cell extract, and a plurality of oligonucleotides;

(b) comparing the presence of ligated oligonucleotides obtained from step (a) with ligated oligonucleotides from a control reaction mixture without the test compound;

(c) determining the effect of the test compound on DNA-dependent protein kinase activity; and

(d) selecting the test compound that results in fewer ligation products in step (a) than in a control reaction mixture without the test compound and does not completely inhibit DNA-dependent protein kinase activity.

25. The method of claim 24, wherein the oligonucleotides are labeled with a detectable marker.

26. The method of claim 24, wherein DNA-dependent protein kinase activity is determined by measuring the phosphorylation of p53 peptide.

27. A single chain antibody comprising an organelle localization signal sequence, wherein the single chain antibody inhibits DNA repair by binding to a DNA repair polypeptide.

28. The single chain antibody of claim 27, wherein the organelle localization signal is selected from the group consisting of a nuclear localization signal and a chloroplast localization signal.

29. The single chain antibody of claim 27, wherein the DNA repair polypeptide is DNA-PKcs.

30. The single chain antibody of claim 29, wherein the single chain antibody binds DNA-PKcs in a region outside the catalytic domain.

31. The single chain antibody of claim 30, wherein the region includes the sequence KKKYIEIRKEAREAANGDSDGPSYM (SEQ. ID NO.:16) or a portion thereof.

32. A single chain antibody comprising a protein transduction domain.

33. The single chain antibody of claim 32, wherein the single chain antibody binds to a DNA repair polypeptide.

34. The single chain antibody of claim 33, wherein the DNA repair polypeptide comprises DNA-PK.

35. The single chain antibody of claim 34, wherein the single chain antibody binds to a region of the DNA-PK polypeptide outside the catalytic domain.

36. The single chain antibody of claim 35, wherein the single chain antibody binds to a region including the sequence KKKYIEIRKEAREAANGDSDGPSYM (SEQ. ID NO.:16) or a portion thereof.

37. A pharmaceutical composition comprising a single chain antibody that binds to a polypeptide comprising the sequence KKKYIEIRKEAREAANGDSDGPSYM (SEQ. ID NO.:16).

38. A pharmaceutical composition of claim 37, wherein the single chain antibody comprises a protein transduction domain and an organelle localization signal.

39. The pharmaceutical composition of claim 38, wherein the organelle localization signal is selected from the group consisting of a nuclear localization signal and a chloroplast localization signal.

40. A vector comprising a promoter operably linked to a polynucleotide encoding a polypeptide comprising a single chain antibody that binds to DNA-PKcs in a region outside of the catalytic domain, a nuclear localization signal, and a protein transduction domain.

41. The vector of claim 40, wherein the promoter is inducible.

42. A method for treating cancer comprising:

introducing into a cancer cell a polypeptide comprising a single chain antibody that binds to DNA-PKcs in a region outside of the catalytic domain operably linked to a nuclear localization signal, wherein said polypeptide inhibits DNA end joining; and

exposing the cancer cell to an amount of ionizing radiation in an amount sufficient to induce breaks in the cancer cell's DNA.

43. A method for treating cancer comprising:

introducing into a cancer cell a polynucleotide encoding a single chain antibody that binds to DNA-PKcs in a region outside of the catalytic domain which is operably linked to a nuclear localization signal and a protein transduction domain, wherein said single chain antibody inhibits DNA end joining by binding DNA-PKcs; and

inducing DNA breaks in the cancer cell.

44. The method of claim 43, wherein the DNA breaks are induced by exposing the cancer cell to ionizing radiation.

45. A method for increasing radiation sensitivity of a cell, comprising:
introducing into the cell a DNA repair modulator, wherein the DNA repair modulator sterically inhibits a DNA repair polypeptide.

46. The method of claim 45, further comprising the step of exposing the cell to radiation.

47. The method of claim 46, wherein the radiation comprises ionizing radiation.

48. The method of claim 45, wherein the DNA repair modulator comprises a polypeptide.

49. The method of claim 48, wherein the polypeptide binds to DNA-PKcs.

50. The method of claim 49, wherein the polypeptide binds outside of the catalytic domain.

51. The method of claim 50, wherein the polypeptide binds to a region comprising the sequence KKKYIEIRKEAREAANGDSDGPSYM (SEQ. ID NO.:16) or a portion thereof.

52. A cell transfected with a vector comprising a promoter operably linked to a polynucleotide encoding a polypeptide comprising a single chain antibody that binds to DNA-PKcs.

53. The cell of claim 52, wherein the cell is stably transfected with the vector.

54. The cell of claim 52, wherein in the polynucleotide is stably integrated into the cell's genome.

55. The cell of claim 52, wherein the vector is episomal.

56. The cell of claim 52, wherein the promoter is inducible.

57. The cell of claim 52, wherein the polypeptide further comprises a nuclear localization signal.

58. The cell of claim 52, wherein the polypeptide binds to a second polypeptide comprising the sequence KKKYIEIRKEAREAANGDSDGPSYM (SEQ. ID NO.:16) or a portion thereof.

59. A method of sensitizing a cell to radiation comprising contacting the cell with a DNA repair modulator, wherein the DNA repair modulator combines with a DNA repair polypeptide to form an aggresome and thereby inhibits DNA repair.

60. A method for inducing cell death comprising contacting the cell with the composition of claim 1 and inducing cell death by exposing the cell to an amount of ionizing radiation sufficient to induce double-strand breaks in the cell's DNA.